TRANSITIONING FROM MANUAL TO STIRRED-TANK BIOREACTOR MANUFACTURING OF IDCT, AN ALLOGENEIC CELL THERAPY TO TREAT LUMBAR DEGENERATIVE DISC DISEASE

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DiscGenics is a clinical stage regenerative medicine company focused on developing cell therapies that alleviate pain and restore function in patients with degenerative disc disease (DDD), a major cause of low back pain which is a driver of disability worldwide. The Company's lead product candidate, IDCT, is a homologous, allogeneic, off-the-shelf, injectable cell therapy under investigational use in the US (ClinicalTrials.gov Identifier: NCT03347708). The manufacturing process for IDCT involves isolating cells from donated intervertebral disc tissue and expanding them into proprietary progenitor cells known as discogenic cells. For preclinical and early clinical testing, cell production was a manual process which relied on pooling individual flasks to achieve the desired lot size. For successful scale-up and commercial production, DiscGenics seeks to modify the IDCT manufacturing process to utilize one large, single vessel per lot, while also applying bioprocess controls and more robust analytical methods to ensure consistent and optimal production of drug product. Once these changes are implemented, the product critical quality attributes (CQAs) must be maintained. DiscGenics has engaged GE Healthcare (GEHC) and the Centre for Commercialization of Regenerative Medicine (CCRM) for assay, media, and process development at the Centre for Advanced Therapeutic Cell Technologies (CATCT) in Toronto, ON., Canada. In partnership with the Federal Economic Development Agency for Southern Ontario (FedDev Ontario), CATCT accelerates the development, industrialization, and adoption of cell manufacturing technologies to improve patient access to cell and gene therapies. In this collaborative project, discogenic cells were generated in traditional static culture using CellStacks (Corning), in PBS-MINI bioreactor systems (PBS Biotech), and in stirred-tank reactors (STRs) (Eppendorf), which was led by the GEHC/CCRM team. Parameters such as cell viability, fold growth, and identity via flow cytometry were compared across modalities. For the STRs, multiple control parameters were evaluated to improve cell growth and assess successful maintenance of a consistent environment for cell quality. In this study, we found that we are able to maintain CQAs between the production modalities, with cell growth being significantly improved in the STR platform. In the STRs, in-process measurements of metabolites aligned with cell growth found using a custom sampling method. Increased cell expansion was facilitated by modified agitation, inoculation, and perfusion feeding strategies. Additionally, the process-controlled STRs provide non-invasive, continuous process data monitoring which allow for development of specified control ranges of manufacturing parameters. The quality by design (QbD) approach taken for the STR process development and improvement has allowed an increase in the lot size, process knowledge, and data-driven process definition. This presentation describes the approach and benefits of transitioning from a manual process to a suspension-based, process-controlled, stirred-tank reactor to produce allogeneic cell therapies.